I. Remarks

After entry of the amendment, claims 2-8, 10-17, 19-31, 33-40 and 104-106 are pending. Claim 1 has been canceled without prejudice.

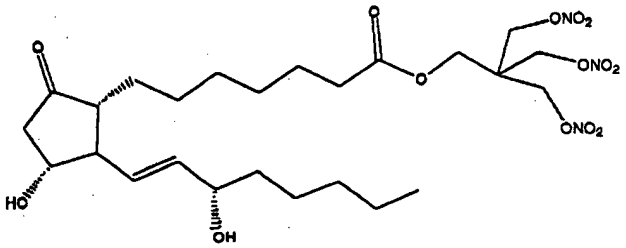
The specification and claim 25 have been amended to correct the formula for N-oxo-N-nitrosamines. One skilled in the art would easily recognize that there was a typographical error in the Formula for N-oxo-N-nitrosamines.

No issues of new matter should arise and entry of the amendment is respectfully requested.

II. Elected Species

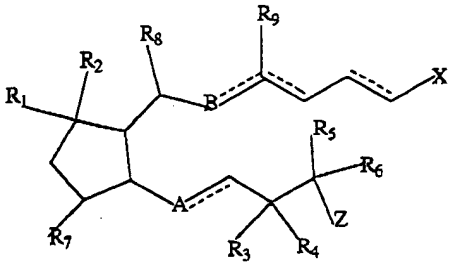
In the discussion between Special Programs Examiner Tsang and the undersigned, Special Programs Examiner Tsang requested that the Applicants identify exactly how the elected species falls within the scope of the compound of Formula (I).

The elected species has the following structure:



A

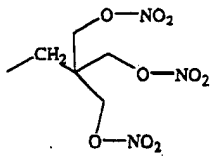
The claimed compounds of Formula (I) have the following structure:



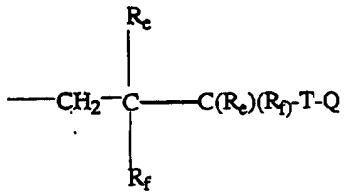
(I)

Application No. 09/516,194
Appendix 1 – Pending Claims

Below is a Table that shows how the elected species falls within the scope of the claimed compound of Formula (I) (see specification at, for example, page 17, line 16 to page 20, line 23.

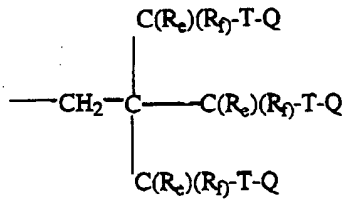
Claimed Compound of Formula I	Elected Species
R_1 and R_2 taken together	=O
R_3	Hydrogen
R_4	$-OD_1$, wherein D_1 is a hydrogen
R_5	Hydrogen
R_6	Hydrogen
R_7	$-OD_1$, wherein D_1 is a hydrogen
R_8	Hydrogen
R_9	Hydrogen
A	-CH=
B	$-CH_2$
Z	Butyl
X	$-C(O)OR_{11}$
R_{11}	D_1, wherein D_1 is D; and D is K
K	

K is $-W_a-E_b-(C(R_e)(R_f))_p-E_c-(C(R_e)(R_f))_x-W_d-(C(R_e)(R_f))_y-W_i-E_j-W_g-(C(R_e)(R_f))_z-T-Q$; for the elected species; wherein a, b, p, c, x, d, i, j and g are each the integer 0; y is the integer 1; and z is the integer 2, such that K is: $-(C(R_e)(R_f))-(C(R_e)(R_f))-(C(R_e)(R_f))-T-Q$;
wherein R_e and R_f at the first occurrence are each a hydrogen;
K is:



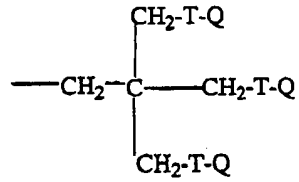
wherein R_e and R_f at the first occurrence are each $-(C(R_e)(R_f))_k$-T-Q; and k is the integer 1;

K is:



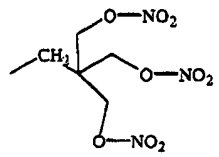
wherein R_e and R_f at the each occurrence is a hydrogen;

K is:



wherein T at each occurrence is an oxygen, and Q at each occurrence is $-NO_2$;

K is:



Applicants respectfully submit that the elected species falls within the scope of the compound of Formula (I) of pending claim 2. If Special Programs Examiner Tsang has any questions about this, she is encouraged to contact the undersigned.

III. "Misjoinder" of Invention

The Examiner objects to claims 2-8, 10-17, 19-31, 33-40 and 104-106 as being directed to a misj inder of nitro and nitroso.

Applicants respectfully submit that there claimed compounds of formula (I) could easily contain both an -NO and an $-NO_2$ group.

Referring to the elected species discussed above, the elected species could also contain an -NO group if the R_7 substituent was $-OD_1$; and D_1 was Q; and Q was -NO.

Alternatively, the elected species could also contain an -NO group if the R_3 substituent was $-OD_1$, and D_1 was Q; and Q was -NO.

Alternatively, the elected species could also contain an -NO group if the R_5 substituent was $-OD_1$, and D_1 was Q; and Q was -NO.

Alternatively, the elected species could also contain an -NO group if the R_6 substituent was $-OD_1$, and D_1 was Q; and Q was -NO.

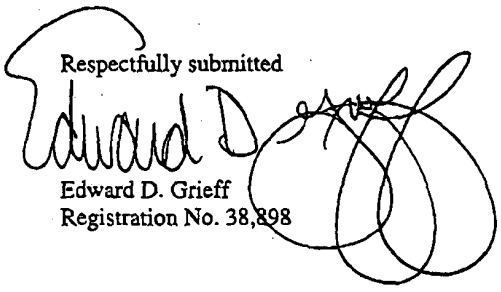
Applicants respectfully submit that it was unreasonable for the Examiner to restrict the claims to either nitro or nitroso when, in fact, the compound of formula (I) can contain nitro and nitroso groups at the same time. The Examiner has completely ignored the compounds of formula (I) that contain both an -NO and an -NO2 group.

In view thereof, Applicants respectfully submit that the pending claims are in condition for allowance.

IV. Conclusion

Applicants respectfully request reconsideration and allowance of pending claims 2-8, 10-17, 19-31, 33-40 and 104-106.

Respectfully submitted



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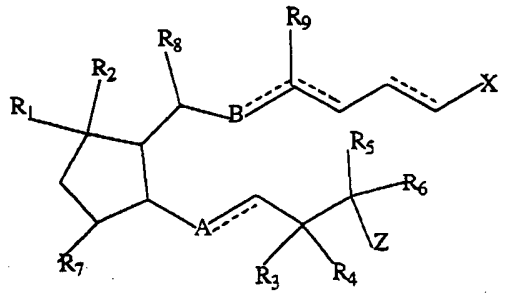
Registration No. 38,898

Date: July 22, 2002
HALE and DORR LLP
1455 Pennsylvania Avenue, NW
Washington, DC 20004
Phone: 202-942-8400

Appendix 1 Pending Claims

2. (Twice Amended) A compound of formula (I) or a pharmaceutically acceptable salt thereof, wherein the compound of formula (I) is:

B1



(I)

wherein the dotted lines indicate a single or a double bond;

R_1 is $-OD_1$ or –Cl;

R_2 and R_8 are a hydrogen; or R_1 and R_2 taken together are $=CH_2$ or =O;

R_3 and R_4 are each independently a hydrogen, $-OD_1$ or $-CH_3$;

R_5 and R_6 are each independently a hydrogen, $-OD_1$, $-CH_3$, $-OCH_3$ or $-CH=CH_2$;

R_7 is a hydrogen or $-OD_1$;

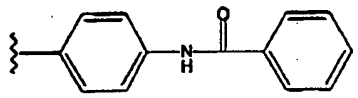
R_9 is hydrogen or absent when the carbon to which it is attached is the central carbon of an allene functionality; or R_8 and R_9 taken together with the chain to which they are attached form a substituted benzene ring with the proviso that R_1 is an oxygen atom which is attached to the carbon atom at the position of the benzene ring defined by B;

A is –CH=, $-CH_2$, -S-, or -O-;

B is –CH=, $-CH_2$, -S-, or –C(O)-;

X is $-CH_2OR_{11}$, $-C(O)OR_{11}$ or $-C(O)N(D_1)R_{12}$;

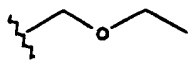
R_{11} is D_1, a lower alkyl group, or



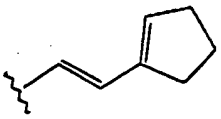
R_{12} is $-S(O)_2CH_3$ or $-C(O)CH_3$;

Z is (a) an ethyl, (b) a butyl, (c) a hexyl, (d) a benzyl,

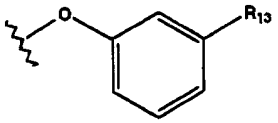
(e)



(f)

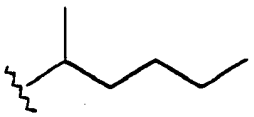


(g)



(h)

or



R_{13} is a hydrogen or –Cl;

D_1 is a hydrogen or D; with the proviso that at least one D_1 in formula (I) must be D;

D is Q or K;

Q is -NO or $-NO_2$;

K is $-W_a-E_b-(C(R_e)(R_f))_p-E_c-(C(R_e)(R_f))_x-W_d-(C(R_e)(R_f))_y-W_i-E_j-W_g-(C(R_e)(R_f))_z-T-Q$; with the proviso that when X is $-C(O)OD_1$ and D_1 is K, then K is not an alkyl, branched alkyl or cycloalkyl mononitrate; a benzoic acid substituted benzyloxy mononitrate; the regioisomeric esters of glycerol dinitrate and oligomers thereof;

a, b, c, d, g, i and j are each independently an integer from 0 to 3;

p, x, y and z are each independently an integer from 0 to 10;

W at each occurrence is independently -C(O)-, -C(S)-, -T-, $-(C(R_e)(R_f))_h-$, an alkyl group, an aryl group, a heterocyclic ring, an arylheterocyclic ring, or $-(CH_2CH_2O)_q-$;

E at each occurrence is independently -T-, an alkyl group, an aryl group, $-(C(R_e)(R_f))_h-$, a heterocyclic ring, an arylheterocyclic ring, or $-(CH_2CH_2O)_q-$;

h is an integer form 1 to 10;

q is an integer from 1 to 5;

R_e and R_f are each independently a hydrogen, an alkyl, a cycloalkoxy, a halogen, a hydroxy, an hydroxyalkyl, an alkoxyalkyl, an arylheterocyclic ring, an alkylaryl, a cycloalkylalkyl, a heterocyclicalkyl, an alkoxy, a haloalkoxy, an amino, an alkylamino, a dialkylamino, an arylamino, a diarylamino, an alkylarylamino, an alkoxyhaloalkyl, a haloalkoxy, a sulfonic acid, a sulfonic ester, an alkylsulfonic acid, an arylsulfonic acid, an arylalkoxy, an alkylthio, an arylthio, a cycloalkylthio, a cycloalkenyl, a cyano, an aminoalkyl, an aminoaryl, an aryl, an arylalkyl, an alkylaryl, a carboxamido, a alkylcarboxamido, an arylcarboxamido, an amidyl, a carboxyl, a carbamoyl, a carbamate, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarbonyl, an arylcarbonyl, an ester, a carboxylic ester, an alkylcarboxylic ester, an arylcarboxylic ester, a haloalkoxy, a sulfonamido, an alkylsulfonamido, an arylsulfonamido, a sulfonic ester, a urea, a phosphoryl, a nitro, -T-Q , or $(C(R_e)(R_f))_k$-T-Q, or R_e and R_f taken together with the carbons to which they are attached form a carbonyl, a methanthial, a heterocyclic ring, a cycloalkyl group or a bridged cycloalkyl group;

k is an integer from 1 to 3;

T at each occurrence is independently a covalent bond, a carbonyl, an oxygen, $-S(O)_o-$ or $-N(R_a)R_i-$;

o is an integer from 0 to 2;

R_a is a lone pair of electrons, a hydrogen or an alkyl group;

R_i is a hydrogen, an alkyl, an aryl, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarboxylic ester, an arylcarboxylic ester, an alkylcarboxamido, an arylcarboxamido, an alkylaryl, an alkylsulfinyl, an alkylsulfonyl, an arylsulfinyl, an arylsulfonyl, a sulfonamido, a carboxamido, a carboxylic ester, an amino alkyl, an amino aryl, $-CH_2-C(T-Q)(R_e)(R_f)$, or $-(N_2O_2-)^-\bullet M^+$, wherein M^+ is an organic or inorganic cation; with the proviso that when R_i is $-CH_2-C(T-Q)(R_e)(R_f)$ or $-(N_2O_2)^-\bullet M^+$, or R_e or R_f are T-Q or $(C(R_e)(R_f))_k$-T-Q, then the "-T- Q" subgroup can be a hydrogen, an alkyl, an alkoxy, an alkoxyalkyl, an aminoalkyl, a hydroxy, a heterocyclic ring or an aryl group.

3. The compound of claim 2, wherein the compound comprising at least one NO group, at least one NO_2 group, or at least one NO and NO_2 group is a nitrosated arbaprostil, a nitrosylated arbaprostil, a nitrosated and nitrosylated arbaprostil, a nitrosated alprostadil, a

nitrosylated alprostadil, a nitrosated and nitrosylated alprostadil, a nitrosated beraprost, a nitrosylated beraprost, a nitrosated and nitrosylated beraprost, a nitrosated carboprost, a nitrosylated carboprost, a nitrosated and nitrosylated carboprost, a nitrosated cloprostenol, a nitrosylated cloprostenol, a nitrosated and nitrosylated cloprostenol, a nitrosated dimoxaprost, a nitrosylated dimoxaprost, a nitrosated and nitrosylated dimoxaprost, a nitrosated enprostil, a nitrosylated enprostil, a nitrosated and nitrosylated enprostil, a nitrosated enisoprost, a nitrosylated enisoprost, a nitrosated and nitrosylated enisoprost, a nitrosated fluprostenol, a nitrosylated fluprostenol, a nitrosated and nitrosylated fluprostenol, a nitrosated fenprostalene, a nitrosylated fenprostalene, a nitrosated and nitrosylated fenprostalene, a nitrosated gemeprost, a nitrosylated gemeprost, a nitrosated and nitrosylated gemeprost, a nitrosated latanaprost, a nitrosylated latanaprost, a nitrosated and nitrosylated latanaprost, a nitrosated limaprost, a nitrosylated limaprost, a nitrosated and nitrosylated limaprost, a nitrosated meteneprost, a nitrosylated meteneprost, a nitrosated and nitrosylated meteneprost, a nitrosated mexiprostil, a nitrosylated mexiprostil, a nitrosated and nitrosylated mexiprostil, a nitrosated misoprostol, a nitrosylated misoprostol, a nitrosated and nitrosylated misoprostol, a nitrosated misoprost, a nitrosylated misoprost, a nitrosated and nitrosylated misoprost, a nitrosated misoprostol acid, a nitrosylated misoprostol acid, a nitrosated and nitrosylated misoprostol acid, a nitrosated nocloprost, a nitrosylated nocloprost, a nitrosated and nitrosylated nocloprost, a nitrosated ornoprostil, a nitrosylated ornoprostil, a nitrosated and nitrosylated ornoprostil, a nitrosated prostalene, a nitrosylated prostalene, a nitrosated and nitrosylated prostalene, a nitrosated PGE_1, a nitrosylated PGE_1, a nitrosated and nitrosylated PGE_1, a nitrosated PGE_2, a nitrosylated PGE_2, a nitrosated and nitrosylated PGE_2, a nitrosated PGF_1, a nitrosylated PGF_1, a nitrosated and nitrosylated PGF_1, a nitrosated $PGF_{2\alpha}$, a nitrosylated $PGF_{2\alpha}$, a nitrosated and nitrosylated $PGF_{2\alpha}$, a nitrosated rioprostil, a nitrosylated rioprostil, a nitrosated and nitrosylated rioprostil, a nitrosated rosaprostol, a nitrosylated rosaprostol, a nitrosated and nitrosylated rosaprostol, a nitrosated remiprostol, a nitrosylated remiprostol, a nitrosated and nitrosylated remiprostol, a nitrosated sulprostone, a nitrosylated sulprostone, a nitrosated and nitrosylated sulprostone, a nitrosated trimoprostil, a nitrosylated trimoprostil, a nitrosated and nitrosylated trimoprostil, a nitrosated tiprostanide, a nitrosylated tiprostanide, a nitrosated and nitrosylated tiprostanide, a nitrosated unoprostone, a nitrosylated unoprostone, a nitrosated and nitrosylated unoprostone, a nitrosated viprostol, a nitrosylated viprostol, a nitrosated and nitrosylated viprostol or a mixture

thereof.

4. A composition comprising the compound of claim 2 and a pharmaceutically acceptable carrier.

5. A method for treating a sexual dysfunction in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 4.

6. The method of claim 5, wherein the patient is female.

7. The method of claim 5, wherein the patient is male.

8. The method of claim 5, wherein the composition is administered orally, by intracavernosal injection, by transurethral application, or by transdermal application.

10. The composition of claim 4, further comprising at least one vasoactive agent or a pharmaceutically acceptable salt thereof.

11. The composition of claim 10, wherein the vasoactive agent is a potassium channel activator, a calcium channel blocker, an □blocker, a □blocker, a phosphodiesterase inhibitor, adenosine, an ergot alkaloid, a vasoactive intestinal peptide, a dopamine agonist, an opioid antagonist, an endothelin antagonist or a mixture thereof.

12. The composition of claim 10, wherein the vasoactive agent is an α-blocker or a phosphodiesterase inhibitor.

13. The composition of claim 12, wherein the α-blocker is phentolamine, prazosin, doxazosin, terazosin, yohimbine or moxisylyte and the phosphodiesterase inhibitor is papaverine, zaprinast, sildenafil or IC 351, or a mixture thereof.

14. A method for treating a sexual dysfunction in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 10.

15. The method of claim 14, wherein the patient is female.

16. The method of claim 14, wherein the patient is male.

17. The method of claim 14, wherein the composition is administered orally, by intracavernosal injection, by transurethral application or by transdermal application.

19. A composition comprising at least one compound of claim 2 or a pharmaceutically acceptable salt thereof, and at least one compound that donates, transfers or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase.

20. The composition of claim 19, further comprising a pharmaceutically acceptable

carrier.

21. The composition of claim 19, wherein the compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor or is a substrate for nitric oxide synthase is an S-nitrosothiol.

22. The composition of claim 21, wherein the S-nitrosothiol is S-nitroso-N-acetylcysteine, S-nitroso-captopril, S-nitroso-N-acetylpenicillamine, S-nitroso-homocysteine, S-nitroso-cysteine or S-nitroso-glutathione.

23. The composition of claim 21, wherein the S-nitrosothiol is:

(i) $HS(C(R_e)(R_f))_mSNO$;

(ii) $ONS(C(R_e)(R_f))_mR_c$; and

(iii) $H_2N\text{-}CH(CO_2H)\text{-}(CH_2)_m\text{-}C(O)NH\text{-}CH(CH_2SNO)\text{-}C(O)NH\text{-}CH_2\text{-}CO_2H$;

wherein m is an integer from 2 to 20; R_e and R_f are each independently a hydrogen, an alkyl, a cycloalkoxy, a halogen, a hydroxy, an hydroxyalkyl, an alkoxyalkyl, an arylheterocyclic ring, an alkylaryl, a cycloalkylalkyl, a heterocyclicalkyl, an alkoxy, a haloalkoxy, an amino, an alkylamino, a dialkylamino, an arylamino, a diarylamino, an alkylarylamino, an alkoxyhaloalkyl, a haloalkoxy, a sulfonic acid, a sulfonic ester, an alkylsulfonic acid, an arylsulfonic acid, an arylalkoxy, an alkylthio, an arylthio, a cycloalkylthio, a cycloalkenyl, a cyano, an aminoalkyl, an aminoaryl, an aryl, an arylalkyl, an alkylaryl, a carboxamido, a alkylcarboxamido, an arylcarboxamido, an amidyl, a carboxyl, a carbamoyl, a carbamate, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarbonyl, an arylcarbonyl, an ester, a carboxylic ester, an alkylcarboxylic ester, an arylcarboxylic ester, a haloalkoxy, a sulfonamido, an alkylsulfonamido, an arylsulfonamido, a sulfonic ester, a urea, a phosphoryl, a nitro, -T-Q , or $(C(R_e)(R_f))_k$-T-Q, or R_e and R_f taken together with the carbons to which they are attached form a carbonyl, a methanthial, a heterocyclic ring, a cycloalkyl group or a bridged cycloalkyl group; Q is -NO or $-NO_2$; and T is independently a covalent bond, a carbonyl, an oxygen, $-S(O)_o$- or $-N(R_a)R_i$-, wherein o is an integer from 0 to 2, R_a is a lone pair of electrons, a hydrogen or an alkyl group; R_i is a hydrogen, an alkyl, an aryl, an alkylcarboxylic acid, an aryl carboxylic acid, an alkylcarboxylic ester, an arylcarboxylic ester, an alkylcarboxamido, an arylcarboxamido, an alkylaryl, an alkylsulfinyl, an alkylsulfonyl, an arylsulfinyl, an arylsulfonyl, a sulfonamido, a carboxamido, a carboxylic ester, an amino alkyl, an amino aryl, $-CH_2\text{-}C(T\text{-}Q)(R_e)(R_f)$, or $-(N_2O_2\text{-})^-\bullet M^+$, wherein M^+ is an organic or inorganic cation; with the proviso that when R_i is

$-CH_2-C(T-Q)(R_c)(R_f)$ or $-(N_2O_2-)\bullet M^+$; then "-T-Q" can be a hydrogen, an alkyl group, an alkoxyalkyl group, an aminoalkyl group, a hydroxy group or an aryl group.

24. The composition of claim 19, wherein the compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase, is L-arginine, L-homoarginine, N-hydroxy-L-arginine, nitrosated L-arginine, nitrosylated L-arginine, nitrosated N-hydroxy-L-arginine, nitrosylated N-hydroxy-L-arginine, citrulline, ornithine, glutamine, lysine, polypeptides comprising at least one of these amino acids or inhibitors of the enzyme arginase.

25. (Amended) The composition of claim 19, wherein the compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase is:

B2

(i) a compound that comprises at least one ON-O-, ON-N- or ON-C- group;

(ii) a compound that comprises at least one O_2N-O-, O_2N-N-, O_2N-S- or $-O_2N$-C- group;

(iii) a N-oxo-N-nitrosoamine having the formula: R^1R^2N-N(O-M^+)-NO, wherein R^1 and R^2 are each independently a polypeptide, an amino acid, a sugar, an oligonucleotide, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted hydrocarbon, or a heterocyclic group, and M^+ is an organic or inorganic cation.

26. The composition of claim 25, wherein the compound comprising at least one ON-O-, ON-N- or ON-C- group is an ON-O-polypeptide, an ON-N-polypepetide, an ON-C-polypeptide, an ON-O-amino acid, an ON-N-amino acid, an ON-C-amino acid, an ON-O-sugar, an ON-N-sugar, an ON-C-sugar, an ON-O-oligonucleotide, an ON-N-oligonucleotide, an ON-C-oligonucleotide, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic ON-O-hydrocarbon, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic ON-N-hydrocarbon, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic ON-C-hydrocarbon, an ON-O-heterocyclic compound, an ON-N-heterocyclic compound or a ON-C-heterocyclic compound.

27. The composition of claim 25, wherein compound comprising at least one O_2N-O-, O_2N-N-, O_2N-S- or O_2N-C- group is an O_2N-O-polypeptide, an O_2N-N-polypeptide, an O_2N-S-polypeptide, an O_2N-C-polypeptide, an O_2N-O-amino acid, O_2N-N-amino acid, O_2N-S-amino

acid, an O_2N-C-amino acid, an O_2N-O-sugar, an O_2N-N-sugar, O_2N-S-sugar, an O_2N-C-sugar, an O_2N-O-oligonucleotide, an O_2N-N-oligonucleotide, an O_2N-S-oligonucleotide, an O_2N-C-oligonucleotide, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O_2N-O-hydrocarbon, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O_2N-N-hydrocarbon, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O_2N-S-hydrocarbon, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O_2N-C-hydrocarbon, an O_2N-O-heterocyclic compound, an O_2N-N-heterocyclic compound, an O_2N-S-heterocyclic compound or an O_2N-C-heterocyclic compound.

28. A method for treating a sexual dysfunction in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 19.

29. The method of claim 28, wherein the patient is female.

30. The method of claim 28, wherein the patient is male.

31. The method of claim 28, wherein the composition is administered orally, by intracavernosal injection, by transurethral application or by transdermal application.

33. The composition of claim 19, further comprising at least one vasoactive agent or a pharmaceutically acceptable salt thereof.

34. The composition of claim 33, wherein the vasoactive agent is a potassium channel activator, a calcium channel blocker, an □blocker, a □blocker, a phosphodiesterase inhibitor, adenosine, an ergot alkaloid, a vasoactive intestinal peptide, a dopamine agonist, an opioid antagonist, an endothelin antagonist or a mixture thereof.

35. The composition of claim 34, wherein the vasoactive agent is an α-blocker or a phosphodiesterase inhibitor.

36. The composition of claim 35, wherein the α-blocker is phentolamine, prazosin, doxazosin, terazosin, yohimbine or moxisylyte and the phosphodiesterase inhibitor is papaverine, zaprinast, sildenafil or IC 351, or a mixture thereof.

37. A method for treating a sexual dysfunction in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 33.

38. The method of claim 37, wherein the patient is female.

39. The method of claim 37, wherein the patient is male.

40. The method of claim 37, wherein the composition is administered orally, by intracavernosal injection, by transurethral application or by transdermal application.

104. A kit comprising at least one compound of claim 2 and at least one compound that donates, transfers or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase.

105. The kit of claim 104, wherein the compound of claim 2 and the at least one compound that donates, transfers or releases nitric oxide, induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase are separate components in the kit or are in the form of a composition in the kit.

106. The kit of claim 104, further comprising at least one vasoactive agent.

Appendix 2 – Amendments to Claims

Cancel claim 1, without prejudice.

25. (Amended) The composition of claim 19, wherein the compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase is:

(i) a compound that comprises at least one ON-O-, ON-N- or ON-C- group;

(ii) a compound that comprises at least one O_2N-O-, O_2N-N-, O_2N-S- or -O_2N-C- group;

(iii) a N-oxo-N-nitrosoamine having the formula: [R^1R^2N-N(O-M^+)-NO] $\underline{R^1R^2N\text{-}N(O\text{-}M^+)\text{-}NO}$, wherein R^1 and R^2 are each independently a polypeptide, an amino acid, a sugar, an oligonucleotide, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted hydrocarbon, or a heterocyclic group, and M^+ is an organic or inorganic cation.

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Appendix 3 –Amended Specificati n

The specification at page 30, lines 5-10, now reads as follows:

B3

Another group of NO adducts are N-oxo-N-nitrosoamines that donate, transfer or release nitric oxide and are represented by the formula: $R^1R^2N\text{-}N(O\text{-}M^+)\text{-}NO$, wherein R^1 and R^2 are each independently a polypeptide, an amino acid, a sugar, a modified or unmodified oligonucleotide, a straight or a branched, saturated or unsaturated aliphatic or aromatic, substituted or unsubstituted hydrocarbon, or a heterocyclic group, and M^+ is as defined herein.

Appendix 4 – Amendments to the Specification

Please amend the specification at page 30, lines 5-10, as follows:

Another group of NO adducts are N-oxo-N-nitrosoamines that donate, transfer or release nitric oxide and are represented by the formula: $[R^1R^2\text{-}N(O\text{-}M^+)\text{-}NO]$ $\underline{R^1R^2N\text{-}N(O\text{-}M^+)\text{-}NO}$, wherein R^1 and R^2 are each independently a polypeptide, an amino acid, a sugar, a modified or unmodified oligonucleotide, a straight or a branched, saturated or unsaturated aliphatic or aromatic, substituted or unsubstituted hydrocarbon, or a heterocyclic group, and M^+ is as defined herein.